

PATENT/Docket No. PC 11050A

Serial No. 09/989,933

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AMENDMENTS TO THE SPECIFICATION

1. Please replace lines 27-34 on page 2 with the following amended paragraph:

~~U.S. Patent Application Serial No. 08/107,908 has~~ The art (generally) have described that the N^{pro} coding sequence or the N^{pro} protein of BVDV is not required for virus replication. ~~The application has~~ The art have described the generation of an attenuated BVD virus, "BVDdN1", in which the entire coding sequence for the N^{pro} protein has been deleted from the viral genome. BVDdN1 is infectious in tissue culture and elicits virus neutralizing serum antibodies when vaccinated into cows. Although BVDdN1 can be used as a vaccine against BVDV, BVDdN1 grows in tissue culture at a rate 2-log slower than the parent wild type virus, making the large-scale production of BVDdN1 difficult.

2. Please replace lines 13-23 on page 5 with the following amended paragraph:

It has been shown in ~~the co-pending U.S. Patent Application Serial No. 08/107,908~~ the art that the N^{pro} coding sequence or the N^{pro} protein of BVDV is not essential for replication of the virus. An attenuated BVDV virus ("BVDdN1") has been described therein which carries a deletion of the full coding sequence for N^{pro} in the viral genome. BVDdN1 is less infectious than the parent wild type virus and elicits virus neutralizing serum antibodies when vaccinated into cows. ~~The entire disclosure of U.S. Patent Application Serial No. 08/107,908 is incorporated herein by reference.~~ Although BVDdN1 can be used as a vaccine against BVDV, BVDdN1 grows in tissue culture at a rate about 2-log slower than the parent wild type virus, making the large-scale production of BVDdN1 difficult. Furthermore, the attenuated BVD virus of the present invention replicates faster than BVDdN1 which provides higher immunogenicity for protection.

3. Please replace lines 16-20 on page 13 with the following amended paragraph:

The vaccine compositions of the present invention can also include additional active ingredient such as other vaccine compositions against BVDV, e.g., those described in ~~co-pending Application Serial No. 08/107,908~~, WO 9512682, WO 9955366, U.S. Patent No. 6,060,457, U.S. Patent No. 6,015,795, U.S. Patent No. 6,001,613, and U.S. Patent No. 5,593,873, all of which are incorporated by reference in their entirety.

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4. Please replace lines 6-13 on page 15 with the following amended paragraph:

The DNA sequence of bovine polyubiquitin has been described by Meyers, G., et al. (*Virology*:180, 602-616, 1991) and is present in GenBank (BOVPOUBA, Accession # M62429 M37794). Cloning and introduction of a monomeric ubiquitin into vector pvvNADLd1NS2 involved two rounds of PCR amplification and synthesis of three PCR fragments. Plasmid pvvNADLd1NS2 is a derivative of pvvNADL (an infectious clone of BVDV described in ~~U.S. Patent Application Serial No. 08/107,908~~ the art) in which the coding region of NS2 is deleted. In the first round, PCR fragments 1 and 2 were generated which then served as templates for the second round of PCR amplification resulting in PCR fragment 3 (Figure 1A).

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